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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,952	01/05/2006	Michael R. Yeaman	066742-0040	1470

41552 7590 12/16/2008

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EXAMINER	
CORDERO GARCIA, MARCELA M	
ART UNIT	PAPER NUMBER
1654	
MAIL DATE	DELIVERY MODE
12/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,952	YEAMAN ET AL.	
	Examiner	Art Unit	
	MARCELA M. CORDERO GARCIA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-73* is/are pending in the application.

4a) Of the above claim(s) *18-33,36,37,39-45 and 59-73* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13-17, 34-35, 38, 46, 49-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 February 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I (claims 1-68) in the reply filed on 12 September 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

With respect to the election of species, Applicant has elected SEQ ID NO: 1 and indicated that claims 1, 2, 12 and 34 (in part) and 3-11, 13-17, 35, 38, 46, 49-58 are readable upon. Upon reconsideration, the rest of species are not required.

Claims 1-73 are pending in the application. Claims 1-17, 35, 38, 46, 49-58 are presented for examination on the merits as they read upon SEQ ID NO: 1. Claims 18-34, 36-37, 39-45, 47-48, 59-73 are withdrawn as not drawn to the elected group/species.

Sequence Compliance

Applicant is advised that the application is not in compliance with 37 CFR §§ 1.821-1.825.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR §§ 1.821- 1.825) in order to completely respond to this office action.

Specifically, no sequence listing / CRF have been provided which includes the amino acid sequences presented e.g., in page 54, line 4 and in Figure 12. In order to

satisfy the sequence rules requirements, Applicant needs to provide an amendment to the instant claims and specification to include reference to the appropriate "SEQ ID NO:".

In case of any new sequences not properly identified in the instant specification, Applicant is required to provide a substitute computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, a new or substitute paper copy of that "Sequence Listing", an amendment directing the entry of that paper copy into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. § 1.821(e) or 1.821(f) or 1.821(g) or 1.825(d). The instant specification will also need to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. For rules interpretation Applicant may call (571) 272-2533. See M.P.E.P. 2422.04.

Please direct all replies to the United States Patent and Trademark Office via one (1) of the following:

1. Electronically submitted through EFS-Bio (<http://www.uspto.gov/ebc/efs/downloads/documents.htm>, EFS Submission User Manual - ePave)

2. US Postal Service:
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3. Hand carry, Federal Express, United Parcel Service, or other delivery service:
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Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-17, 34-35, 38, 46 and 49-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level

of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

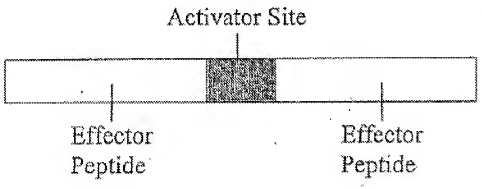
> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See

MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872 F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims are drawn to a context-activated protide comprising at least one activator site and one or more effectors, wherein at least two of said effectors have distinct biological functions.

A context-activated protide is depicted in Figure 1 (disclosure):



With regards to the term "context-activated protide", the disclosure (in the instant patent application publication) at [0007] teaches that "this invention is directed to multifunctional, context-activated protides that have two or more effectors with individually distinct biological functions and one or more corresponding activator sites that can each initiate or amplify the biological function of one or more effectors upon context-activation. The context-activated protides of the invention are useful in the diagnosis, prophylaxis, and therapy of a broad range of pathological conditions. However, the effectors, beyond those in claims 1-2 are only functionally described as being antimicrobial, a chemokine-like peptide effector (IL-8 domain), an so forth ([0027]-[0034]). The biological functions for the effectors can be antimicrobial,

immunomodulatory, tumoricidal, proapoptotic, anti-apoptotic, pro-angiogenic, anti-angiogenic and hemolytic (claim 34). The effector can comprise a peptide or a non-peptide (claims 35-36). The disclosure defines the term "effector" as referring to the peptide or non-peptide functional domains of an invention protide that have specific individual functions, which are initiated or amplified upon activation and achieve specific functions relating to the diagnosis, prevention, or treatment of a disease. As described herein, an invention protide has at least two effector domains with distinct, complementary and/or synergistic biological functions. An effector is inactive or exhibits relatively reduced or attenuated biological activity unless an activator, by virtue of either its presence or absence, alters or facilitates or allows the altering of its corresponding activator site and, as a result, initiates or amplifies the diagnostic, prophylactic, therapeutic, or other biological function(s) of the effector(s). Multiple effectors can be induced by the same activator site. Peptide and non-peptide effectors can be present in the same protide, which can be referred to as a hybrid protide. Similarly, a protide can consist exclusively of peptide effectors, also referred to as a peptide protide. Similarly, a protide of the invention can consist exclusively of non-peptidic effectors. The biological function(s) of an effector that corresponds to an invention protide can be, for example, antimicrobial, immunomodulatory, pro- or anti-inflammatory, tumoricidal, pro- or anti-apoptotic, pro- and anti-angiogenic and/or hemolytic. ([0043)] Although a few sequences (claims 1-2) are expressly claimed, the effectors are also drawn to a variety of peptidomimetics which are known in the art including, for example, peptide-like molecules that contain a constrained amino acid, a non-peptide component that mimics peptide secondary structure, or an amide bond isostere. A peptidomimetic that contains a constrained, non-naturally occurring amino acid can include, for example, an .alpha.-methylated amino acid; an .alpha.,.alpha.-dialkyl-glycine or .alpha.-aminocycloalkane

carboxylic acid; an N.alpha.-C.alpha. cylized amino acid; an N.alpha.-methylated amino acid; a .beta.- or .gamma.-amino cycloalkane carboxylic acid; an .alpha.,.beta.-unsaturated amino acid; a .beta.,.beta.-dimethyl or .beta.-methyl amino acid; a .beta.-substituted-2,3-methano amino acid; an N-C.delta. or C.alpha.-C.delta. cyclized amino acid; or a substituted proline or another amino acid mimetic. In addition, a peptidomimetic that mimics peptide secondary structure can contain, for example, a nonpeptidic .beta.-turn mimic; .gamma.-turn mimic; mimic of .beta.-sheet structure; or mimic of helical structure, each of which is well known in the art. A peptidomimetic also can be a peptide-like molecule which contains, for example, an amide bond isostere such as a retro-inverso modification; reduced amide bond; methylenethioether or methylenesulfoxide bond; methylene ether bond; ethylene bond; thioamide bond; trans-olefin or fluoroolefin bond; 1,5-disubstituted tetrazole ring; ketomethylene or fluoroketomethylene bond or another amide isostere. One skilled in the art understands that an invention protide can encompass these and other peptidomimetics. Likewise, an invention protide also can contain stereoisomeric amino acids or other effector or activator constituents, such as dextrorotatory (D) versions of amino acids ([0038)]. The disclosure goes on to teach that "as described herein, a protide can contain naturally occurring and non-naturally occurring amino acids as well as amino acid analogs and mimetics. Naturally occurring amino acids include the 20 levorotatory(L)-amino acids utilized during protein biosynthesis as well as others such as 4-hydroxyproline, hydroxylysine, desmosine, isodesmosine, homocysteine, citrulline and ornithine, for example. Non-naturally occurring amino acids include, for example, (D)-amino acids, norleucine, norvaline, p-fluorophenylalanine, ethionine and the like. Amino acid analogs include modified forms of naturally and non-naturally occurring amino acids. Such modifications can include, for example, substitution or replacement of chemical groups

and moieties on the amino acid or by derivitization of the amino acid. Amino acid mimetics include, for example, organic structures which exhibit functionally similar properties such as charge and charge spacing characteristic of the reference amino acid. For example, an organic structure which mimics Arginine (Arg or R) would have a positive charge moiety located in similar molecular space and having the same degree of mobility as the .alpha.-amino group of the side chain of the naturally occurring Arg amino acid. Mimetics also include constrained structures so as to maintain optimal spacing and charge interactions of the amino acid or of the amino acid functional groups. Those skilled in the art know or can determine what structures constitute functionally equivalent amino acid analogs and amino acid mimetics useful for preparation of an invention protide." ([0039]).

With respect to the term "context-activated" the disclosure teaches that "the protide of the invention, refers to the initiation, activation or amplification of a biological or other desired, for example, diagnostic or prophylactic function of one or more protide effectors in a particular temporal, spatial, pathological and/or biochemical context. Context-activation can be initiated by direct or indirect interaction between a protide activator site and a corresponding activator that is selectively associated with the particular context. As used herein, context-activation encompasses activation in a wide variety of contexts that can include, for example, local, regional, systemic, and/or temporal proximity; as well as the presence or absence of an etiological agent, pathologic condition, or characteristic components thereof." [(0041)] The term "activator site" : refers to a domain of the protide that, in the presence of an activator, initiates, promotes, amplifies or modulates the specific biological function of one or more effectors. As described herein, an activator site can be modified, cleaved, processed or otherwise altered in the presence of an activator. In addition, an activator site can be

sensitive either to the absolute presence or absence of an activator as well as can be sensitive to a threshold concentration of an activator rather than its mere presence ([0045]). The claims are drawn, not only to peptides but to non-peptidic compounds and peptidomimetics having a host of biological activities, therefore a mere statement that such compounds would be desirable for making protides does not sufficiently provide ample written description pages describing the full breadth of the instantly claimed protides with biological activity as instantly claimed. The specification does provide examples of what qualify as compounds of the claimed invention (see, e.g, Example 1), however, the example is drawn to PT-1 (protide-1) See. Figure 13. Also 3 other protides are described PT-2, PT-3 and PT-4. However, applicant has not shown possession of the genus encompassed by claim 3 and having at least two distinct biological functions as instantly claimed. Please note that [0093]-[0119] describe examples of potential applications of the protides including therapeutic use. However Example 1 is drawn only to in vitro determinations and does not encompass any in vivo testing. As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claim 3 is a broad generic with respect all possible compounds encompassed by the claims. The possible structural variations are limitless to protides which can be formed by peptides or non-peptides with biological activity conjugated via an activator site that can release the peptidic or non-peptidic components, e.g., by enzymatic interaction. It must not be forgotten that the MPEP states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here, though the claims may recite some functional characteristics, the claims lack written

description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the example in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of non-peptidic protides, in vivo acting protides, hybrid protides, peptidic protides and protides encompassing the many biological functions instantly claimed. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 1 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of prior U.S. Patent No. 7,067,621. This is a double patenting rejection. Please note that both inventions are drawn to a context activated protide comprising SEQ ID NO: 1. Therefore the same invention is claimed.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-17, 34-35, 38, 46 and 49-58 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 7,067,621. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are drawn to SEQ ID NO: 1 (claims 1-2) and to functional properties (claims 3-17, 34-35, 38, 46, 49-58) which were admitted by Applicant to be encompassed by the context activated protides comprising / consisting of SEQ ID NO: 1, and which are claimed by patent US '621 (See Applicant's

reply dated 12 September 2008, page 9). Please note that the species (SEQ ID NO: 1) anticipates the genus (as claimed in instant claims 3-17, 34-35, 38, 46 and 49-58).

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCELA M. CORDERO GARCIA whose telephone number is (571)272-2939. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cecilia Tsang/ /Marcela M Cordero Garcia/

Supervisory Patent Examiner, Art Unit 1654 Examiner, Art Unit 1654

MMCG 12/08